30. (New) The transgenic plant of claim 16, wherein the plant is selected from the group consisting of wheat, barley, rice, rape, pea, maize, sugar beet, sugar cane and potato.

A3 cont'd

31. (New) A product harvested from the transgenic plant of claim 27 comprising plant cells.

32. (New) A propagation material comprising the plant cell of claim 14.

REMARKS

Amendments in the Specification

For the convenience of the Examiner, applicants have submitted a substitute specification formatted with paragraph and line numbers. Applicants have amended the specification to recite that this application is a continuation of the earlier PCT application that designates the United States. In order to conform with 37 U.S.C. § 1.77(b), applicants have inserted section titles "Background of the Invention", "Summary of the Invention", "Brief Description of the Drawings" and "Detailed Description of the Invention" in the specification. Applicants have moved the section under "Summary of the Invention" (page 1, lines 3-17) after the section "Background of the Invention" (page 1, line 18 to page 2, line 35). Applicants have also moved the section under "Brief Description of the Drawings" (page 14, line 26 to page 17, line 13) before the section "Detailed

Description of the Invention" (starting on page 3, line 1). In addition, applicants have corrected certain punctuation errors. These amendments are marked in red on copies of pages 1-3, 6 and 14-17 of the specification as originally filed (Appendix 1).

The Claim Amendments

Applicants have amended claims 1, 2-5 and 8-20 to improve their form. Applicants have also amended claim 2 to recite "hybridizes under stringent conditions". Support for this amendment can be found, for example, on page 6, lines 15-19 of the specification as originally filed. Applicants have also amended claim 2 to recite "encoding a polypeptide amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO:2." Support for this amendment can be found, for example, on page 7, lines 9-12 of the specification as originally filed. Applicants have also replaced the phrase "a chemical compound functionally equivalent to 2-deoxyglucose" with the term "a non-metabolizable analogue of glucose" in claims 9 and 10. Support for this amendment can be found on, for example, on page 3, lines 15-16 of the specification as originally filed.

Applicants have further amended claims 4, 5, 8-13 and 15-20 to remove improper multiple dependencies. Applicants have amended claim 19 to include steps a) and b).

Support for this amendment can be found, for example, in claim 10 as originally filed.

The above amendments are listed in Appendix 2.

Applicants have added claims 21, 24-28 and 31-32 which are directed to subject matter transferred from claims 1, 13 and 15-18. Support for the addition of claims 29-30 can be found, for example, on page 14, lines 12-14 of the specification as originally filed. Support for the addition of claims 22-23 can be found in claim 2 as originally filed.

None of the amendments add new matter.

Information Disclosure Statement

The Examiner has initialed and dated a copy of Applicant's Form PTO-1449. The Examiner contends on Form PTO-1449 that Kocourek et al. was not in English and no explanation of relevance was filed. Applicants traverse.

Applicants submitted a Concise Statement of Relevance as Appendix 1 in the Information Disclosure Statement on December 21, 2001. A copy of the December 21, 2001 Information Disclosure Statement and Appendix 1 is enclosed herewith in Appendix 3.

Claim Objections

The Examiner has objected claims 1, 5, 8-10, 13 and 16 because the indefinite article "a" is omitted before the phrases "recombinant DNA molecule", "vector", "host cell",

"kit", "process", "transgenic" and "transgenic plant", respectively.

Applicants have amended claims 1, 5, 8-10, 13 and 16 to insert the article "a" before the above phrases, thereby overcoming the objections.

The Examiner has also objected claim 14 because the definite article "the" is omitted before "plant cell."

Applicants have amended claim 14 to insert the article "the" before "plant cell", thereby overcoming the objection.

The Examiner has objected claims 8-20 because the claims depend on claims of nonelected inventions.

Applicants have amended claims 8-20 to remove their dependencies on nonelected claims 6 and 7, thereby overcoming the objection.

The Examiner has objected to claims 4-5, 8-13 and 15-20 under 37 C.F.R. 1.75 (c) as being in improper form because a multiple dependent claim should refer to other claims in alternative only and/or cannot depend from any other dependent claim.

Applicants have amended claims 4-5, 8-13 and 15-20 to remove improper multiple dependencies, thereby overcoming the objection.

§ 35 U.S.C. 112 First Paragraph Rejections

Claims 1-5, 8-9 and 13-18 are rejected under 35

U.S.C. §112, first paragraph, as containing subject matter that, in the Examiner's view, was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner contends that the instant application provides written description only for a recombinant DNA molecule comprising a DNA sequence encoding 2-deoxyglucose-6-phosphate phosphatase operably linked to plant regulatory sequences, where said DNA sequence encodes SEQ ID NO:2, a vector, a host cell, and transgenic plants and plant cells comprising said recombinant DNA molecule (Examples 1-12 pages 19-24, and Sequence Listing).

The Examiner contends that the instant application does not describe a DNA molecule comprising nucleotide sequences that hybridize to the above-described DNA sequences or that is a derivative, analogue or fragment of said DNA sequences and encodes a protein possessing 2-deoxyglucose-6-phosphate phosphatase activity. The Examiner contends that the specification does not describe which regions of the nucleotide or amino acid sequence are essential for 2-deoxyglucose-6-phosphate phosphatase activity. The Examiner contends that the application does not describe other nucleotide sequences encoding a protein possessing 2-deoxyglucose-6-phosphate phosphatase activity.

The Examiner contends that given the lack of written description in the specification with regard to the structural and physical features of hybridizing sequences or sequences that are a derivative, analogue or fragment of a sequence that encodes a protein possessing 2-deoxyglucose-6-phosphate phosphatase activity, one skilled in the art would not recognize from the disclosure that applicant was in possession of the claimed invention at the time this application was filed (see Written Description Guidelines, Federal Register, Vol.66, No. 4, January 5, 2001, pages 1099-1111).

Claim 1 as amended is directed to a recombinant DNA molecule comprising a regulatory sequence of a promotor active in plants and a DNA sequence encoding a 2-deoxyglucose-6-phosphate phosphatase. At the time of the priority date of the application, several 2-deoxyglucose-6-phosphate phosphatases were known in the art. For example, Randez-Gil (cited below) describes two genes DOG^R1 and DOG^R2 from yeast, each of which encodes a 2-deoxyglucose-6-phosphate phosphatase. In addition, H. Mori (NCBI acession number BAA16133) describes the amino acid sequence of 2-deoxyglucose-6-phosphate phosphatase from *E. Coli*. The application as filed, makes it clear that the invention encompasses the use of 2-DOG-6-P phosphatase in the construct and is not limited to the exemplified 2-DOG-6-P

phosphatase. One of ordinary skill in the art, thus, would believe that applicant's were in possession of the invention as claimed.

Applicants have amended part (c) of claim 2 to recite "hybridizes under stringent conditions." Applicants have also replaced the phrase "a derivative, analogue or fragment" with "encoding a polypeptide amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 2" in part (e) of claim 2. As such, the DNA sequences recited in amended claim 2 are structurally similar DNAs. Thus, a representative number of species is disclosed. Therefore, one skilled in the art would recognize from the disclosure that applicants were in possession of the claimed invention in amended claims 1, 2, 3-5, 8-9 and 13-18 at the time the application was filed.

Claims 1-5 and 8-20 are rejected under 35 U.S.C. § 112, first paragraph as not enabled. The Examiner concedes that the specification enables a recombinant DNA molecule comprising a DNA sequence of SEQ ID NO:1 operably linked to plant regulatory sequences, for a vector, a host cell, a kit, transgenic plants, plant cells, tissue, harvest products and propagation material comprising said recombinant DNA molecule, and for a process for selecting transformed plant cells comprising transforming plants cells with said recombinant DNA molecule and selecting transformed cells on 2-deoxyglucose containing media, use of said recombinant DNA

molecule to produce transgenic plant plants, cells and or tissue, and use of said recombinant DNA molecule as a selectable marker in plant cell and tissue culture. In the Examiner's view, however the specification does not reasonably provide enablement for other recombinant DNA molecules comprising other DNA sequences, or for products comprising said other recombinant DNA molecules, or for processes using said other recombinant DNA molecules.

Specifically, the Examiner asserts that the specification discloses a recombinant DNA molecule comprising a DNA sequence of SEQ ID NO:1 encoding 2-deoxyglucose-6-phosphate phosphatase of SEQ ID NO:2 operably linked to plant regulatory sequences, a vector, a host cell, transgenic tobacco, potato, and pea plants and plant cells comprising said recombinant DNA molecule, and a process for selecting transformed plant cells comprising transforming plants cells with said recombinant DNA molecule and selecting transformed cells on 2-deoxyglucose containing media (Examples 1-12 pages 19-24, and Sequence Listing). The Examiner states that the specification does not disclose how to make and use sequences comprising a nucleotide sequence which hybridizes to (a) or (b), or sequences being a derivative, analogue or fragment of (a), (b), (c) or (d) encoding a protein possessing 2-deoxyglucose-6-phosphate phosphatase activity. The Examiner contends that the application also does not disclose how to make and use other

nucleotide sequences encoding a protein possessing 2-deoxyglucose-6-phosphate phosphatase activity. The Examiner contends that it would require undue experimentation for one of skilled in the art to determine which of those sequences that hybridize to the DNA sequence of SEQ ID NO:1 encode a protein having a 2-deoxyglucose-6-phosphate phosphatase activity. The Examiner also contends that it would require undue experimentation for one of skill in the art to determine the structure of other sequences encoding a protein having a 2-deoxyglucose-6-phosphate phosphatase activity, as the specification provides no guidance as to which nucleotide or amino acid sequence regions are essential to 2-deoxyglucose-6-phosphate phosphatase activity.

As stated above, claim 1 as amended is directed to a recombinant DNA molecule comprising a regulatory sequence of a promotor active in plants and a DNA sequence encoding a 2-deoxyglucose-6-phosphate phosphatase. Amended claim 2 recites "hybridizes under stringent conditions" and "encoding a polypeptide amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 2." The specification does teach how to make and use the sequences in amended claim 1 and 2. See, e.g., on page 4, line 32 to page 5, line 34, page 6, lines 20-30 and page 19, line 11 to page 24, line 20 of the specification as originally filed. In addition, Randez-Gil (cited below) describes the identification of a 2-deoxyglucose-6-phosphate phosphatase

gene, thus it would not require undue experimentation for one skill in the art to determine sequences that encode a 2-deoxyglucose-6-phosphate phosphatase at the time of the priority date of the application.

Further, the specification teaches that the expression of 2-deoxyglucose-6-phosphate phosphatase results in a decrease in 2-deoxyglucose-6-phosphate accumulation in plants. See, e.g., page 22, lines 10-17 of the specification as originally filed. For example, Table 1 of the specification shows that expression of 2-deoxyglucose-6-phosphate phosphatase leads to a decrease in 2-deoxyglucose-6-phosphate accumulation in leaf disks. In addition, transgenic tobacco, potato and pea plants expressing 2-deoxyglucose-6-phosphate phosphatase are resistant against 2-deoxyglucose-6-phosphate containing medium. See, e.g., page 23, lines 4-21 and page 24, lines 13-20 of the specification as originally filed. Thus, one of ordinary skill in the art would be able to routinely determine sequences that encode a 2-deoxyglucose-6-phosphate phosphatase. Thus, claims 1-5 and 8-20 are enabled.

§ 35 U.S.C. 112 Second Paragraph and 101 Rejections

The Examiner contends that claims 1-5 and 8-20 are rejected under § 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and

distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner contends that claim 1 is indefinite in the recitation of "may." The Examiner suggests that the claim be amended to delete the word "may." The Examiner further contends that claim 1 is indefinite in the recitation of "regulatory sequences of a promoter". The Examiner contends that it is unclear whether regulatory sequences of a promoter includes a promoter.

Applicants have amended claim 1 to delete the word "may", thereby overcoming the rejection. The phrase "regulatory sequences of a promotor" is not indefinite since it is clear that it includes a promotor. See, e.g., page 7, lines 32-35 of the specification as originally filed.

The Examiner contends that claim 2 is indefinite in the recitation of "hybridizes to." The Examiner contends that it is unclear under what hybridization conditions would yield the DNA sequences. The Examiner suggests that the claim be amended to recite specific hybridization conditions.

Applicants have amended claim 2 to recite "a DNA sequence which hybridizes under stringent conditions", thereby overcoming the rejection.

The Examiner contends that claim 3 is indefinite in the recitation of "derived." The Examiner contends that it is unclear how much of the DNA sequence is derived from

yeast. The Examiner suggests that the claim be amended to recite "obtained."

Applicants have amended claim 3 to replace the phrase "derived" with the phrase "obtained" as suggested by the Examiner, thereby overcoming the rejection.

The Examiner contends that claim 5 is indefinite in the recitation of the indefinite article "a" before "recombinant DNA molecule". The Examiner suggests that the claim be amended to recite "the recombinant DNA molecule."

Applicants have amended claim 5 to replace "a" with "the" before "recombinant DNA molecule" as suggested by the Examiner, thereby overcoming the rejection.

The Examiner contends that claim 8 is indefinite in the recitation of the transitional phrase "containing." The Examiner suggests that the claim be amended to recite a transitional phrase such as "comprising", "consisting of, or "consisting essentially of." The Examiner also contends that claim 8 is indefinite in the recitation of the indefinite article "a" before "recombinant DNA molecule." The Examiner suggests that the claim be amended to recite "the recombinant DNA molecule."

Applicants have amended claim 8 to replace the word "containing" with "comprising" and to recite "the recombinant DNA molecule" as suggested by the Examiner, thereby overcoming the rejection.

The Examiner contends that claim 9 is indefinite in the recitation of the indefinite article "a" before "recombinant DNA molecule" and before "vector." The Examiner suggests that the claim be amended to recite "the recombinant DNA molecule", and "the vector." The Examiner also contends that claim 9 is indefinite in the recitation of "functionally equivalent to." The Examiner contends that it is unclear in what way the chemical compound is functionally equivalent to 2-deoxyglucose.

Applicants have amended claim 9 to recite "the recombinant molecule" and "a vector comprising said recombinant DNA molecule" to overcome the rejection. Applicants have also replaced the phrase "a chemical compound functionally equivalent to 2-deoxyglucose" with the term "a non-metabolizable analogue of glucose", thereby overcoming the rejection.

The Examiner contends that claim 10 is indefinite in the recitation of the indefinite article "a" before "recombinant DNA molecule." The Examiner suggests that the claim be amended to recite "the recombinant DNA molecule." The Examiner also contends that claim 10 is indefinite in the recitation of "functionally equivalent to." The Examiner contends that it is unclear in what way the chemical compound is functionally equivalent to 2-deoxyglucose.

Applicants have amended claim 10 to recite "the recombinant molecule" as suggested by the Examiner to

overcome the rejection. Applicants have also replaced the phrase "a chemical compound functionally equivalent to 2-deoxyglucose" with the term "a non-metabolizable analogue of glucose", thereby overcoming the rejection.

The Examiner contends that claim 13 is indefinite in the recitation of the transitional phrase "containing." The Examiner contends that the scope of the claim is unclear. The Examiner suggests that the claim be amended to recite a transitional phrase such as "comprising", "consisting of, or "consisting essentially of." The Examiner also contends that claim 13 is indefinite in the recitation of the indefinite article "a" before "recombinant DNA molecule" and before "vector." The Examiner suggests that the claim be amended to recite "the recombinant DNA molecule", and "the vector."

Applicants have amended claim 13 to replace the word "containing" with "comprising" and to recite "the recombinant DNA molecule" and "a vector comprising said recombinant DNA molecule", thereby overcoming the rejection.

The Examiner contends that claim 16 is indefinite in the recitation of the transitional phrase "containing." The Examiner contends that the scope of the claim is unclear. The Examiner suggests that the claim be amended to recite a transitional phrase such as "comprising", "consisting of, or "consisting essentially of." The Examiner also contends that claim 16 is indefinite in the recitation of the indefinite

article "a" before "plant cell." The Examiner suggests that the claim be amended to recite "the plant cell."

Applicants have amended claim 16 to replace the word "containing" with "comprising" and to recite "the plant cell" as suggested by the Examiner, thereby overcoming the rejection.

The Examiner contends that claims 19 and 20 are indefinite in the recitation of the indefinite article "a" before "DNA sequence", "recombinant DNA molecule" and "vector." The Examiner suggests that the claims be amended to recite "the DNA sequence", "the recombinant DNA molecule", and "the vector." The Examiner contends that claims 19 and 20 provide for the use of a DNA sequence. The Examiner contends that since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. In the Examiner's view, claims 19 and 20 are rejected under 35 § U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process.

Applicants have amended claim 19 to delete the phrase "a DNA sequence", to recite "the recombinant DNA molecule", "a vector comprising said recombinant DNA molecule" and steps a) and b), thereby overcoming the rejection. Applicants have amended claim 20 to recite "the recombinant DNA molecule", to delete the phrases "a DNA

sequence" and "a vector", and to depend from amended claim 1 or 2, thereby overcoming the rejection.

§ 35 U.S.C. 103 Rejections

Claims 1-5 and 8-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Randez-Gil et al., Yeast, Vol. 11, pages 1233-1240 (1995) (herein after "Randez-Gil") in view of Herrera-Estrella et al. EMBO Journal, Vol. 2, pages 987-995 (1983) (herein after "Herrera-Estrella", and in further view of Zemek et al. Z. Pflanzenphysiol. Bd., Vol. 76, pages 114-119 (1975) (hereinafter "Zemek I") and Zemek et al. Z. Pflanzenphysiol. Bd., Vol. 77, pages 95-98 (1976) (hereinafter "Zemek II".

Specifically, the Examiner asserts that Randez-Gil teaches a recombinant DNA molecule comprising a DNA sequence of SEQ ID NO:1 encoding 2-deoxyglucose-6-phosphate phosphatase of SEQ ID NO:2 that functions to inactivate 2-deoxyglucose, operably linked to yeast regulatory sequences, a host cell, transgenic yeast cells, tissue, a process for selecting transformed yeast cells comprising transforming yeast cells with said recombinant DNA molecule and selecting transformed cells on 2-deoxyglucose containing media, use of said recombinant DNA molecule to produce transgenic yeast cells, and use of said recombinant DNA molecule as a selectable marker in yeast cell culture (page 1236 Table 1). The Examiner concedes, however, that

Randez-Gil does not teach a recombinant DNA molecule comprising a DNA sequence encoding 2-deoxyglucose-6-phosphate phosphatase operably linked to plant regulatory sequences*, or processes or products involving the transformation and selection of plant cells. The Examiner further asserts that Herrera-Estrella teaches processes and products involving the transformation and selection of plant cells using recombinant DNA molecules encoding microbial enzymes that function to inactivate compounds that inhibit the growth of plant cells in cell culture (page 987 abstract), that Zemek I teaches that 2-deoxyglucose inhibits the growth of tobacco callus tissue culture (page 118 Figure 3), and that Zemek II teach that 2-deoxyglucose inhibits the growth of spruce tissue culture (page 96 Figure 1).

In the Examiner's view, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to use the recombinant DNA molecule comprising a DNA sequence encoding 2-deoxyglucose-6-phosphate phosphatase from yeast Randez-Gil, to transform plant cells, for the purpose of selecting transformed cells on 2-deoxyglucose containing media and producing transformed plants, without any surprising or unexpected results. The

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* Applicants would like to clarify that the instant invention refers to "regulatory sequences of a promotor active in plants" and not "plant regulatory sequences." See, claim 1 as originally filed.

Examiner contends that one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Applicants traverse.

One skilled in the art would not have been motivated to combine Randez-Gil, Herrera-Estrella, Zemek I and II and generate the claimed invention with reasonable expectation of success. Specifically, none of Herrera-Estrella, Zemek I and II mentions the 2-deoxyglucose-6-phosphate phosphatase gene. Although Randez-Gil refers to the DNA sequence of SEQ ID NO:1 encoding the 2-deoxyglucose-6-phosphate phosphatase of SEQ ID NO:2 from yeast, it teaches away from combining the above references to generate the claimed invention with reasonable expectation of success. Randez-Gil recites that the actual function of 2-deoxyglucose-6-phosphate phosphatase in regular yeast metabolism is not known. See, e.g., page 39, column 1, last paragraph of Randez-Gil. Thus, further investigation of 2-deoxyglucose-6-phosphate phosphatase is required, and therefore one skilled in the art would never have thought of combining the above references and using the phosphatase in an organism foreign to yeast, let alone in plants.

Further, none of Zemek I, II and Randez-Gil teach a recombinant DNA molecule comprising a DNA sequence encoding 2-deoxyglucose-6-phosphate phosphatase operably linked to a regulatory sequence of a promotor active in plants, or processes or products involving the transformation and

selection of plant cells on 2-deoxyglucose containing medium. Herrera-Estrella only refers to processes and products involving the transformation and selection of plant cells using recombinant DNA molecules encoding *aminoglycoside phosphotransferase or methotrexate-insensitive dihydrofolate reductase*. It does not suggest using the recombinant DNA molecule comprising a DNA sequence encoding *2-deoxyglucose-6-phosphate phosphatase* to transform and select plant cells. In addition, Herrera-Estrella teaches away from combining the above references since the methods described in Herrera-Estrella were not always effective and frequently negatively affected plant regeneration (page 2, lines 23-24 of the specification as originally filed). None of the above references teach or suggest using a 2-deoxyglucose-6-phosphate phosphatase as a selection marker in plants. None of the above references teach or suggest detoxifying a metabolic intermediate product, 2-deoxyglucose-6-phosphate, which is derived from 2-deoxyglucose. In coming to the conclusion that the claimed invention would have been *prima facie* obvious as a whole to one ordinary skilled in the art the time the invention was made, the Examiner is clearly engaging in hindsight reconstruction.

Thus, claims 1-5 and 8-20 are not obvious in view of Randez-Gil, Herrera-Estrella, Zemek I and II.

CONCLUSION

Applicants request entry of the amendments and allowance of the claims.

Respectfully submitted,

Jane T. Gunnison (Reg. No. 38,479)
Attorney for Applicants
Li Su (Reg. 45,141)
Agent for Applicants
c/o FISH & NEAVE
1251 Avenue of the Americas
New York, New York 10020
Tel.: (212) 596-9000
Fax.: (212) 596-9090

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